Biodistribution of systemically administered PEG-PLys(fructose)-BPA in subcutaneous mouse tumor models was examined using ICP-MS, and intratumoral distribution of PEG-PLys(fructose)-BPA was observed by CLSM. For the study of tumor suppression, thermal/epithermal neutrons were irradiated to tumors 3 and 6 hours after intravenous injection of polymer-BPA.

Results

PEG-PLys(fructose) with narrow molecular weight distribution was synthesized successfully (Mw of PEG: 10, 000, polymerization degree of PLys: 57, fructose introduction rate: 57.8 %), and it augmented the water-solubility of BPA.

The cellular uptake of PEG-PLys(fructose)-BPA was higher than conventional boron drug, and was decreased by 54% upon addition of system L inhibitor, suggesting that PEG-PLys(fructose)-BPA can target LAT-1 and be efficiently taken up by the cancer cells. CLSM study showed that the polymer-BPA was taken up into cells by endocytosis through LAT-1 transporter and remained in the endosome. Taken together, PEG-PLys(-fructose)-BPA should be internalized into the cancer cells via LAT-1 mediated endocytosis.

In in vivo study, PEG-PLys(fructose)-BPA showed drastically higher tumor accumulation than conventional fructose-BPA complexes and maintained high boron concentration for 6 h. Ultimately, in the study of tumor suppression, 18 days after thermal neutron irradiation, PEG-PLys(fructose)-BPA significantly suppressed the tumor growth without apparent side effects compared to the fructose-BPA complexes.

Conclusion

PEG-PLys(fructose)-BPA exhibited high accumulation and prolonged retention within the tumor, and exerted significantly enhanced BNCT effect compared with the conventional fructose-BPA complexes. PEG-PLys(fructose)-BPA has a great potential for clinical use in BNCT..

Keyword: BPA, fructose, functional polymer, LAT1, endocytosis

Pa P1 01

Accelerator Neutron Source for in-vitro and in-vivo BNCT studies

Sergey Taskaev[1,2*], Timophey Bykov[1,2], Dmitrii Kasatov[1,2], Iaroslav Kolesnikov[1,2], Alexey Koshkarev[1,2], Alexandr Makarov[1,2], Yuri Ostreinov[1,2], Ivan Shchudlo[1,2], Eugeniya Sokolova[1,2], Igor Sorokin[1,2]

[1]*Budker Institute of Nuclear Physics*
[2]*Novosibirsk State University, Novosibirsk, Russia*
E-mail: taskaev@inp.nsk.su

Introduction
A source of epithermal neutrons based on vacuum-insulated tandem accelerator and a lithium target was proposed and developed for the technique of boron neutron capture therapy. A stationary proton beam of 2 MeV with a current of up to 6 mA was obtained in the accelerator. Neutron generation was performed and the flux and neutron spectrum were experimentally measured.

Materials and Methods
The work was carried out on an accelerating neutron source created at the Budker Institute of Nuclear Physics. The accelerator was equipped with wire scanner OWS-30 (D-Pace), non-contact current sensor Bergoz, infrared camera FLIR, pyrometer, cooled diaphragms to ensure long-term stable operation. The source of neutrons provides the epithermal neutron flux density to 3 108 cm-2 s-1. The test cell cultures or mice are placed inside a plexiglas phantom mounted on a rotating table. The neutron flux is monitored by a neutron detector based on the GS20 scintillator (Saint-Gobain Crystals) and a set of activation foils SWX-1552 (Shieldwerx). The total neutron yield is measured by target activation with beryllium-7. The absorbed dose is determined by performing numerical calculations of neutron transport and gamma radiation by the Monte Carlo method. For carrying out biological studies, the unit is equipped with an atomic emission spectrometer ICPE-9820 (Shimadzu) and other necessary equipment.

Results
The effect of a space charge and aberrations of a focusing magnetic lens on a beam of negative hydrogen ions injected into accelerator was discovered. Taking into account, this effect and visualization of the ion beam made it possible to ensure a stable long-term operation of the accelerator with high current. The x-ray and gamma-radiation dose rates and spectra and the neutron-emission dose rate upon the absorption of 2-MeV protons in various materials have been measured along with the residual-activity radiation spectrum. In situ observation of blistering of samples prepared from copper and tantalum was performed during their irradiation with a 2-MeV proton beam. The results of these studies determined the design of the neutron-generating target. A series of biological studies were carried out together with a number of Russian and Japanese scientific organizations. It was established that neutron irradiation of tumor cells, previously incubated in a medium with boron, led to a significant suppression of their viability. Irradiation of mice with

grafted human glioblastoma tumor led to their complete cure. A new method for measuring the absorbed dose based on the activation of stable nuclei introduced into the composition of the targeted delivery of boron is proposed and tested. A beam shaping assembly was developed and manufactured, which makes it possible to form a therapeutic beam of neutrons at 2.3 MeV proton energy to the greatest extent satisfying the requirements of BNCT.

Conclusion

The accelerator neutron source created at the Budker Institute of Nuclear Physics provides a beam of epithermal neutrons and provides an opportunity to conduct research in the field of BNCT. The results of biological studies have confirmed the acceptable quality of the neutron beam. At present, the neutron source is being modernized to produce a therapeutic neutron beam to the greatest extent satisfying the requirements of BNCT.

Keyword: accelerator, lithium target, epithermal neutrons

Pa P1 02

In Situ Observations of Blistering of a Metal Irradiated with 2-MeV Protons

Sergey Taskaev[1,2*], Alexander Badrutdinov[3], Timophey Bykov[1,2], Sergey Gromilov[2,4], Yasuo Hugashi[3], Dmitrii Kasatov[1,2], Iaroslav Kolesnikov[1,2], Alexey Koshkarev[1,2], Alexandr Makarov[1,2], Takuya Miyazawa[3], Ivan Shchudlo[1,2], Andrey Shoshin[1,2], Evgeniia Sokolova[1,2], Hirotaka Sugawara[3]

[1]*Budker Institute of Nuclear Physics, Novosibirsk, Russia*
[2]*Novosibirsk State University, Novosibirsk, Russia*
[3]*Okinawa Institute of Science and Technology Graduate University, Onna-son, Okinawa, Japan*
[4]*Nikolaev Institute of Inorganic Chemistry, Novosibirsk, Russia*
E-mail: taskaev.sergey@gmail.com

Introduction

In accelerator neutron sources for BNCT, neutron generation is performed by dumping a proton beam onto a target. In most cases the target is a thin layer of lithium or beryllium deposited on the structural metal. With irradiation of the target by protons, deformation of the surface layer occurs in the form of numerous blisters, which leads to a decrease in thermal conductivity and limits the time of operation. Experimental data on the critical dose of blistering have been extremely scarce and are absent for a proton energy of about